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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,994	07/28/2003	Leslie Baumann	81301.0001	4265

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WILEY, REIN & FIELDING, LLP
ATTN: PATENT ADMINISTRATION
1776 K. STREET N.W.
WASHINGTON, DC 20006

EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,994	BAUMANN ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-21 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *December 17, 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This application was filed July 28, 2003. Claims 11-22 and 27-29 are pending in this application and examined on the merits herein.

Election/Restrictions

Applicant's provisional election with traverse of group I, drawn to a method of treating aged or photo-damaged skin by administering a composition consisting essentially of 1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine or a biologically active derivative thereof, filed August 17, 2006, is acknowledged. Applicant's arguments of record with respect to the aforementioned traversal are acknowledged and found to be convincing to remove the requirement for restriction between groups II and III but not between I and II or III. Specifically, the invention of group I is directed to a different patient population and outcome than that of groups II and III. Group I is directed toward a screening method for determining the efficacy of a compound, while groups II and III are directed toward therapeutic and diagnostic methods. A screening method is performed on experimental subjects who in many cases are animals with experimentally induced disease, while clinical methods are practiced on subjects, usually human, suffering from disease from other causes. A therapeutic method utilizes whichever therapy or combination of therapies is deemed most likely to successfully treat the disorder, while a screening method utilizes methods and compositions of unknown efficacy in order to determine their level of efficacy. A therapy has as its endpoint the clinical improvement of a patient's condition, while a screen has as its endpoint the

identification of a particular useful composition, without regard to the state of the experimental subjects. For these reasons, the relevant literature for group I is separate and distinct from that for groups II-III. For example, a reference disclosing a screen for useful dermatological compositions may not disclose any actual useful compositions, and a reference disclosing that a particular useful composition or therapeutic method is useful for treating a particular disorder may not disclose a general method for screening for additional compositions. For these reasons the examination of all groups together imposes an additional search burden on the office. Therefore the requirement for restriction is maintained and made **FINAL**.

Claims 1-10 and 23-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **with** traverse in the reply filed on August 17, 2006.

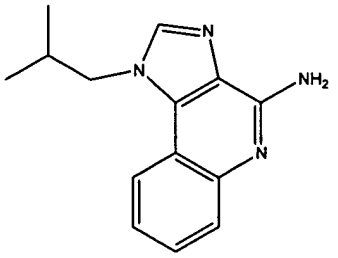
Claims 11-22 and 27-29 are pending in this application and examined on the merits herein.

Claim Rejections - 35 USC § 112

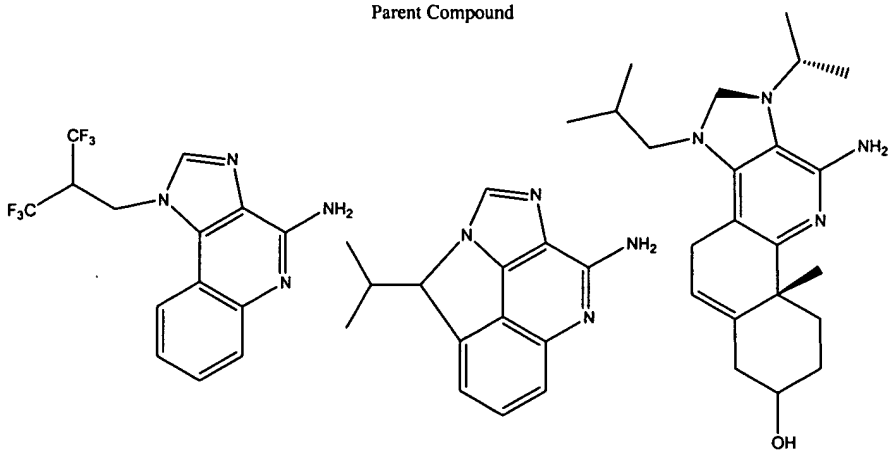
The following is a quotation of the second paragraph of 35 U.S.C. 112:

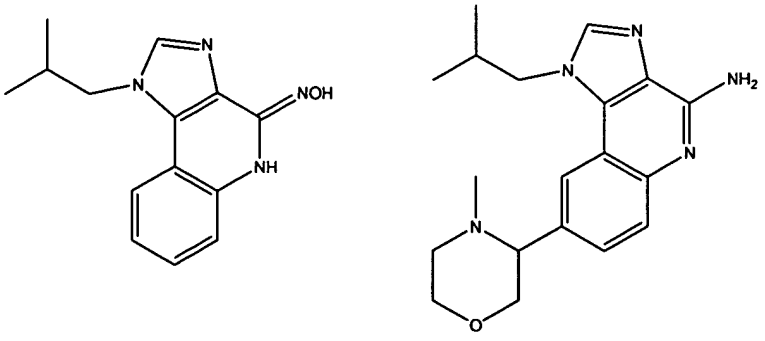
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 12, 14, and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the limitation, "1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine or a biologically active derivative thereof." This limitation fails to clearly and distinctly identify what is a biologically active derivative of the disclosed compound. For example, all, some, or none of the following compounds may reasonably be considered to be derivatives:



Parent Compound





Possible Derivatives

Although Paragraph 0018 of the specification discloses certain particular embodiments of the term "biologically active derivative," the examples given are not presented as limiting the scope of the claims. Therefore the specification fails to define this term.

Furthermore, the term, "biologically active," fails to define the range of *in vivo* effects considered to render a particular compound biologically active. In particular, it is not clear if the biological effects must involve the skin or whether other systemic effects are included in the scope of this limitation. For these reasons, claim 11, and its dependant claims 12, 14, and 19-21, are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11, 13, 14, 19-21, 27, and 28, are rejected under 35 U.S.C. 102(b) as being anticipated by Stockfleth et al. (Reference included with PTO-892) Stockfleth et al. discloses a method of treating actinic keratosis, a non-malignant, precancerous lesion of the skin caused by aging or excessive UV exposure. (p. 1050, left column, first paragraph) The method comprises administering a 5% imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) cream 2-3 times a week to the affected area, and

successfully removed the lesions without recurrence. (p. 1051, right column, last paragraph – p. 1052, left column, second paragraph) This treatment regimen is identical to that disclosed in instant claims 11, 13, 14, and 19-21. During treatment, the AK lesions became inflamed (erythema) and were clearly visible by visual assessment. (p. 1052, left column, third paragraph, p. 1051, figure 1, particularly frames B and C) Stockfleth et al. also discloses that this inflammatory response may be used as a clinical marker to indicate the initiation of an immune response. Although Stockfleth et al. does not explicitly state that the applied composition attracts macrophage cells to the area, activates the toll-like receptor 7, or identifies a precancerous region of skin, all of these elements are inherent in the method as disclosed by Stockfleth et al. The steps disclosed in the reference are the same as in the instant claims, administering the same compound in the same amounts to the same or similar cells or subjects by the same mode of administration. See *Ex parte Novitski* 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3c. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it relates to the claimed invention herein.

The claimed invention is thus anticipated by Stockfleth et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 15-18, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stockfleth et al. (Reference included with PTO-892) Stockfleth et al. discloses a method of treating actinic keratosis, a non-malignant, precancerous lesion of the skin caused by aging or excessive UV exposure. (p. 1050, left column, first paragraph) The method comprises administering a 5% imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) cream 2-3 times a week to the affected area, and successfully removed the lesions without recurrence. (p. 1051, right column, last paragraph – p. 1052, left column, second paragraph) This treatment regimen is identical to that disclosed in instant claims 11, 13, 14, and 19-21. During treatment, the AK lesions became inflamed (erythema) and were clearly visible by visual assessment. (p. 1052, left column, third paragraph, p. 1051, figure 1, particularly frames B and C) Stockfleth et al. also discloses that this inflammatory response may be used as a clinical marker to indicate the initiation of an immune response. Stockfleth et al. does not specifically disclose a method comprising daily administration of imiquimod, or administration of imiquimod in a composition comprising 1-2% or 1.25% imiquimod.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Stockfleth et al. administering the imiquimod daily in a concentration of 1-2% or 1.25%. One of ordinary skill in the art would have been motivated to modify the invention in this way because the method as practiced by Stockfleth et al. leads to a significant inflammatory response which causes discomfort

and inconvenience. Therefore a lower dose administered more frequently would be expected to lead to less severe irritation. One of ordinary skill in the art would reasonably have expected success because adjusting the dosage level and frequency of administration is well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 11-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maibach et al. (US patent application 10/178082, cited in PTO-892) Maibach et al. discloses a method for treating hyperpigmentation of the skin resulting from various causes including UV exposure or age (paragraph 0006, 0016, 0017) comprising administering an active agent selected from a number of compounds including proinflammatory agents such as imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) in combination with various skin penetration enhancers. (paragraph 0092) The composition is preferably administered in one or more doses per day. (paragraph 0130) In two examples given of therapeutic methods, changes in skin appearance are measured by photographic assessment. Two examples of pharmaceutical formulations are given including 1% hydroquinone as the active agent. Maibach et al. does not specifically disclose methods involving a composition consisting essentially of imiquimod, or compositions consisting essentially of 1.25%, 1-2%, or 5% imiquimod.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Maibach et al. using imiquimod as the active ingredient. It would also have been obvious to one of ordinary skill in the art to use a

composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod, as described by instant claims 13 and 15-18. One of ordinary skill in the art would have been motivated to use imiquimod as the active ingredient because Maibach recites imiquimod as one possible active ingredient for use in the invention. One of ordinary skill in the art would have been motivated to use a composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod because the examples given by Maibach et al. consist essentially of 1% active agent, which is within the approximate range of these values. One of ordinary skill in the art would have reasonably expected success in using imiquimod because Maibach discloses that the invention will work with imiquimod, and would have reasonably expected success in using a composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod because determining the precise amounts of active ingredient to apply is well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Summary

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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9/1/06

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